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10/825,607	04/16/2004	Kevin John Slater	4730.00015	8055

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EXAMINER	
SHEN, BIN	
ART UNIT	**PAPER NUMBER**
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/825,607	SLATER ET AL.	
	Examiner	Art Unit	
	BIN SHEN	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 44-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34, 44-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 1-34, 44-54 are considered on the merits.

Claim Objections

Claim 52 objected to because of the following informalities: on line 12, "ratio" was misspelled. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-24, 33, 44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting the presence of contaminating mycoplasma in a mammalian cell culture, does not reasonably provide enablement for any test samples with bacteria and certain eukaryotic microbes growth (such as fungi, see Ingram-Smith et al. Trend in Microbiology 2006;14(6):249-253). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The specification as filed, is enabled for a method of detecting the presence of mycoplasma in a mammalian cell culture sample, but is not enabled for any test sample especially samples with bacteria and/or eukaryotic microbes (such as fungi) growth.

The art of biotechnology is a highly unpredictable art and it would be an undue burden for one of ordinary skill in the art to test any and all kind of test sample to see if mycoplasma can be detected by measuring acetate/carbamate kinase. It is clear that the claimed detection method

can only detect mycoplasma in mammalian cell culture, and can not detect mycoplasma in any test sample especially samples with bacteria and/or eukaryotic microbes (such as fungi) growth, thus one of ordinary skill in the art would not know how to practice the detection method in just any test sample.

Applicant has only stated in their example that bacteria have acetate kinase activity are not those that are commonly found as contaminants of cell culture, (see specification at page 26), and did not address how to separate test samples with eukaryotic microbe growth. It is clear that such broad claims are not enabled by the instant specification when one of ordinary skill in the art practice the detection method with any test samples.

Thus, the claims are unduly broad and do not find proper support from the instant specification. Thus, the rejection is properly made.

Applicant's arguments filed 5/23/2008 have been fully considered but they are not persuasive.

Applicant argues that no evidence is cited for the presence of bacteria or eukaryotic microbes (fungi) in a sample, and that to the extent there are other microbes that could potentially complicate the assay method, one skilled in the art recognized that the techniques for accommodating them would be the same as those used for bacteria.

It is the examiner's position that Ingram-Smith was provided for the presence of bacteria or eukaryotic microbes (fungi) in a sample, and the claims rejected under 35 USC 112, first paragraph provide no step of separating mycoplasma and bacterial (or fungi) cells. Further, although Ingram-Smith does not demonstrate the actual activity of acetate kinase, they do demonstrate that the gene encoding acetate kinase is present in fungi. Hence, a person of ordinary skill in the art would reasonably expect that the eukaryotic fungi would have the acetate kinase activity because they have genes encoding the enzyme in their genome. Accordingly, the mere finding of acetate kinase activity is not definitive that mycoplasma are present in a sample. It would not be unusual that a cell culture could get contaminated by fungi.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 10, 13, 14, 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Kahane (1978).

Kahane teaches a mycoplasma acetate kinase activity assay comprises providing a test sample (page 143, left column, under Materials and Methods) detecting/measuring the appearance/ disappearance of one or more of the substrates/products of acetate kinase in mycoplasma as claimed in claim 3 after osmotically lysis (page 143, Materials and Methods and Results and Discussion, 1st and 2nd paragraph), wherein the method measuring ATP (page 144, Table 1 and 2), wherein ADP is added as substrate (acetyl phosphate, page 143, right column, line 9) to the test sample prior to the measuring step (page 144, Table 2).

Therefore, the cited reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-34, 44-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Kahane et al. (FEMS Microbiology Letters 1978;3:143-145) in view of Ito et al. (Analytical Sciences 2003;19:105-109).

Kahane teaches what is above.

Kahane does not teach the detection of mycoplasma in cell culture and the assay reaction is a bioluminescent reaction

Ito teaches a bioluminescent measurement of acetate kinase (Title and abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make use of Kahane's conclusion that mycoplasmas has acetate kinase activity to develop a detection method by measuring acetate kinase activity and combine Ito's bioluminescent method to simplify the detection method because both methods teach acetate kinase assays. One would have been motivated to make the modification because Kahane et al. specifically described the acetate kinase assay and that acetate kinase presents in mycoplasma and Ito et al. teach the advantages of the bioluminescent method, and would reasonably have expected success in view of Ito's teaching that no interference in the measurement of the acetate kinase and with good sensitivity when using their bioluminescent method (page 107, 1st full paragraph). The choice of detecting mycoplasma in cell culture using enzyme activity ratio of testing sample over control sample, the adjustment of particular conventional working conditions (e.g., use of detergent, incubation time period for the reaction, choice of cell lines) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan having the cited reference before him/her.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed 5/23/2008 have been fully considered but they are not persuasive.

Applicant argues that Kahane does not detect whether mycoplasma is present in the sample.

It is the examiner's position that Kahane is cited for teaching an acetate kinase assay and establishing acetate kinase's presence in mycoplasma (page 143, left column, last line of 1st paragraph), which is required for the developing of a detecting method by measuring acetate kinase activity. To establish a method of detecting the presence of mycoplasma by measuring acetate/carbamate kinase activity, it is necessary to show not only acetate kinase present in

mycoplasma, but also acetate kinase is unique to mycoplasma (which applicant fails to provide support in the specification). Furthermore, the intended use of the method for detecting the presence of "contaminating" mycoplasma does not materially change the steps in the method, thus does not carry patentable weight. "Contamination" is a value-laden word that does not distinguish between a sample that has accidental presence of mycoplasma from a sample where the mycoplasma have been placed there on purpose.

Applicant argues that a skilled worker presented with Kahane would have no reason to to use the method of Kahane on cell culture and run a control sample and compare the results of that control sample with a second measurement.

It is the examiner's position that mycoplasma contamination in the cell culture is well known in the art. A skilled worker upon reading Kahane, would also have recognized the desirability to detect mycoplasma with Kahane's assay with predictable results since a person of ordinary skill has good reason to pursue the known options within his or her technical grasp (using a control sample to compare the different measurements is a routine practice and is well within the grasp of a person of ordinary skill).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, Ph.D., whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571) 272-0925.

B Shen

Art Unit 1657

/JON P WEBER/

Supervisory Patent Examiner, Art Unit 1657